Support for newly added claim 25 is found on page 9 lines 26-29. Herein it is stated that the invention " covers the use of isolated or recombinant DNA or fragments thereof" "which were isolated using cDNA encoding a CTLA-8 protein as a probe.".

Newly added claims 26 and 27 claim nucleic acids that encode peptides that are at least 75% homologous to SEQ ID Nos.: 2, 4, 6, 8, or 10. Support for these claims is found on page 29, lines 8-20 wherein typical homologous proteins or peptides are defined as having from 25-100% homology to 50-100% homology depending on the methods by which the sequences are compared and homology is evaluated. Further, in the carryover paragraph of pages 17-18, the meaning of substantial homology between nucleotide sequences is defined. In lines 25-29 it is stated that "Substantial homology...means...that the segments...when compared, are identical when optimally aligned...in at least about 50% of the nucleotides". One can calculate that nucleotide sequences that share 50% sequence homology can code for proteins that are 75% identical. Further support for newly added claim 26 is implicit in the discussion of the observed 60% homology between the murine CTLA-8 gene and its homologs in humans and herpesvirus samurai on page 9, lines 32-36. One can easily calculate that genes that share 60% nucleotide sequence homology can encode proteins that share 90% sequence identity.

Support for newly added claim 28 is found on page 17, line 9 wherein it is stated that "recombinant clones derived from genomic sequences, e.g., containing introns, will be useful for transgenic studies".

Support for newly added claim 29 is found on page 22, lines 25-26 wherein it is stated that "Expression vectors...containing the desired...gene or its fragments" are "operably linked to suitable genetic control elements that are recognized in a suitable host cell".

Support for newly added claims 30 and 32 is found on page 23 lines 10-12. Herein it is stated that the invention contemplates the use of "expression vectors which are capable of expressing eukaryotic cDNA coding for a CTLA-8 protein in a prokaryotic or eukaryotic host". Thus, the newly added claims are supported by the specification. On page 22, lines 31-36 and continuing over to the next page, the genetic control elements of the subject expression vectors are described: "the genetic control elements can include a prokaryotic promoter system or a eukaryotic promoter expression control system, and typically include a transcriptional promoter, ...suitable ribosome binding site, and sequences that terminate transcription and translation". Thus, the specification also supports newly added claims 31 and 33.

Support for newly added claim 34, 35 and 37 is found on page 24 lines 31-35. These claims define the types of cells in which the expression vector may be propagated and expressed. In the specification, some of the cell types that can be employed in the practice of this invention are yeasts (line 31), insect cells (line 34), and mammalian cells (line 35). Support for newly added claim 36 is found on page 26, line 1 wherein the word "baculovirus" appears. The use of yeast as a host cell is further supported in the discussion on page 25, lines 15-33. The types of mammalian cells that can be employed in the practice of this invention are further specified on page on page 26, lines 6-9 providing support for newly added claim 38: "Examples of useful cell lines include...Chinese hamster ovary(CHO) cell lines, baby rat kidney (BRK) cell lines, ...and monkey (COS) cell lines."

Support for newly added claim 39 is found on page 23, lines 19-24. Herein it is pointed out that it is "not always necessary that an expression vector replicate in a host cell" thus, the newly added claim 39 is provided for in the specification.

On page 26, lines 30-32, explicit support for newly added claim 40 is provided. The applicants discuss the desirability of "express[ing] a CTLA-8 protein polypeptide in a system which provides a specific or defined glycosylation pattern", and on page 32, lines 33-36 it is noted that "Particularly preferred means for accomplishing this are by exposing the polypeptide to glycosylating enzymes derived from cells which normally provide such processing". This leads to support for newly added claim 41, wherein a particular method for providing glycosylating enzymes is claimed. The support for newly added claim 41 can be found on page 26, line 31-32 wherein the applicants say that "the CTLA-8 protein gene may be co-transformed with one or more genes encoding mammalian or other glycosylating enzymes".

Support for newly added claim 42, 43, 44 and 45 is found on page 50, within lines 12-18. In the practice of the invention, the applicants note that the invention may involve the use of "oligonucleotide or polynucleotide sequences taken from the sequence of a CTLA-8 protein. These sequences can be used as probes for detecting levels of antigen message in samples from patients suspected of having an abnormal condition, ...The preparation of both DNA and RNA nucleotide sequences... has received ample description and discussion in the literature". Support for use of the words "cellular proliferation" is found on page 2 of the specification in lines 1 and 3. Support for the term inflammation is found for example, in original claim 5 which recites secretion of an "inflammatory mediator". It would be understood that an inflammatory mediator mediates inflammation.

Thus, all of the newly added claims are supported by the specification. No new material is added.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

MARKED-UP VERSION OF THE CHANGES TO THE CLAIMS

IN THE CLAIMS:

1. (amended) An isolated nucleic acid [at least 95% identical to one] encoding a mammalian CTLA protein or fragment thereof.

CLAIMS APPENDIX
(current wording of all pending claims)

1. (amended) An isolated nucleic acid encoding a mammalian CTLA protein or fragment thereof.

2. The nucleic acid of claim 1, wherein said encoding nucleic acid comprises a sequence of SEQ ID NO: 1, 3, 5, 7, or 9.

23. (new) The isolated nucleic acid of claim 1, wherein the protein induces an inflammatory mediator such as IL-6, IL-8 or PGE2.

24. (new) A nucleic acid sequence that hybridizes under stringent conditions to a nucleic acid sequence of claim 2 or fragment thereof.

25. (new) A nucleic acid isolated using a cDNA encoding a nucleic acid of claim 2 or fragment thereof as a probe.

26. (new) A nucleic acid that encodes a polypeptide that is at least 75% identical to SEQ ID No.: 2, 4, 6, 8, or 10.

27. (new) A nucleic acid that encodes a polypeptide that is at least 90% identical to SEQ ID No.: 2, 4, 6, 8, or 10.

28. (new) The nucleic acid of claim 26, wherein the coding sequence is interrupted by introns.

29. (new) A recombinant expression system for a nucleic acid comprising a nucleic acid expression vector wherein the nucleic acid of claim 26 is operably linked to suitable genetic control elements that are recognized in a suitable host cell.

30. (new) The expression system of claim 29 wherein the host cell is a prokaryotic cell.

31. (new) The expression system of claim 29 wherein the genetic control elements are comprised of a prokaryotic promoter system, prokaryotic ribosome binding site, and a prokaryotic transcription termination signal.

32. (new) The expression system of claim 29 wherein the host cell is a eukaryotic cell.

33. (new) The expression system of claim 29 wherein the genetic control elements are a eukaryotic promoter system, a eukaryotic ribosome binding site, and eukaryotic transcription termination and polyadenylation signals.

34. (new) The expression system of claim 29 wherein the host cell is a yeast cell.

35. (new) The expression system of claim 29 wherein the host cell is an insect cell.

36. (new) The expression system of claim 29 wherein the expression vector is an insect baculovirus expression vector.

37. (new) The expression system of claim 29 wherein the host cell is a mammalian cell.

38 (new) The expression system of claim 29 wherein the host cell is a chinese hamster ovary (CHO) cell, a monkey (COS) cell, or a baby rat kidney (BRK) cell.

39. (new) The expression system of claim 29 wherein the expression vector does not replicate (autonomously) in the host cell.

40. (new) The expression system of claim 29 wherein the expression vector is transformed into a cell which provides a specific glycosylation pattern.

41. (new) The expression system of claim 29 wherein the expression vector is co-transformed into a cell with one or more genes encoding mammalian or other glycosylating enzymes.

42. (new) A method for diagnosing patients suspected of having an abnormal condition wherein a sample from a patient is contacted with a nucleic acid that encodes a polypeptide which is at least 90% identical to SEQ ID No.: 2, 4, 6, 8, or 10.

43. (new) The method of claim 42, wherein the abnormal condition is:

a.) inflammation or;

b.) a disorder involving cellular proliferation.

44. (new) The method of claim 42 wherein the nucleic acid is RNA.

45. (new) The method of claim 42 wherein the nucleic acid is DNA.